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Per- and polyfluoroalkyl substances in sera from children 3 to 11 years of age participating in the National Health and Nutrition Examination Survey 2013–2014

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Abstract

Several per- and polyfluoroalkyl substances (PFAS) have been measured in U.S. National Health and Nutrition Examination Survey (NHANES) participants 12 years of age and older since 1999–2000, but PFAS data using NHANES individual samples among children younger than 12 years do not exist. To obtain the first nationally representative PFAS exposure data in U.S. children, we quantified serum concentrations of 14 PFAS including perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS), and perfluorononanoic acid (PFNA), in a nationally representative subsample of 639 3–11 year old participants in NHANES 2013–2014. We used on-line solid-phase extraction coupled to isotope dilution-high performance liquid chromatography-tandem mass spectrometry; limits of detection were 0.1 ng/mL for all analytes. We calculated geometric mean concentrations, determined weighted Pearson correlations, and used linear regression to evaluate associations of sex, age (3–5 vs 6–11 years), race/ethnicity (Hispanic vs non-Hispanic), household income, and body mass index with concentrations of PFAS detected in more than 60% of participants. We detected PFOS, PFOA, PFHxS, and PFNA in all children at concentrations similar to those of NHANES 2013–2014 adolescents and adults, suggesting prevalent exposure to these PFAS or their precursors among U.S. 3–11 year old children, most of whom were born after the phase out of PFOS in the United States in 2002. PFAS concentration differences by sex, race/ethnicity, and age suggest lifestyle differences that may impact exposure, and highlight the importance of identifying exposure sources and of studying the environmental fate and transport of PFAS.

Keywords

Biomonitoring; Exposure; NHANES; PFAS

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ijheh.2017.09.011>.

1. Introduction

Per- and polyfluoroalkyl substances (PFAS) have been in use for over 60 years in a variety of industrial and commercial applications, such as surfactants, lubricants, paper and textile coatings, polishes, food packaging, and fire-retarding foams (ATSDR, 2015; DeWitt, 2015; Lau et al., 2007; Prevedouros et al., 2006). Because of their chemical inertness and heat stability, several PFAS persist and bioaccumulate in the environment, and certain PFAS, such as perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS), are ubiquitous contaminants detected worldwide in occupationally exposed workers and general populations, as well as in wildlife (ATSDR, 2015; DeWitt, 2015).

Considerable amount of animal data suggest potential adverse health effects related to exposure to PFOA and PFOS (other PFAS have not been evaluated as extensively) including hepatotoxicity, tumor induction, developmental toxicity, immunotoxicity, neurotoxicity, and endocrine disruption (Corsini et al., 2012, 2014; DeWitt, 2015; Kennedy et al., 2004; Lau et al., 2004, 2007). However, the relevance of these animal data for human health is somewhat unclear because of the much shorter half-life of PFAS in animals compared to humans, and the possible dependence of toxicity on a peroxisome proliferation mechanism likely to be not as important in humans (DeWitt, 2015; Grandjean and Clapp, 2014; Steenland et al., 2010). Because animals and humans sometimes process chemicals differently, additional research will help scientists fully understand how PFAS may affect human health.

Epidemiologic research findings on the potential health effects from exposure to PFAS in humans, albeit inconsistent, cover a wide spectrum of outcomes, mainly associated with exposures to PFOA and PFOS, including increased serum cholesterol, low-density lipoprotein and uric acid, thyroid, cardiovascular and kidney diseases, altered liver enzyme activities, lengthened time-to-pregnancy, early onset of menopause, delays in age of menarche, abnormal fetal growth and development, attention deficit hyperactivity disorder, and reduced immune responses in children, (Apelberg et al., 2007; ATSDR, 2015; DeWitt, 2015; Fei et al., 2007, 2008, 2010; Granum et al., 2013; Gump et al., 2011; Hamm et al., 2010; Lopez-Espinosa et al., 2011; Nolan et al., 2009; Olsen et al., 2009; Stein et al., 2014; Stein and Savitz, 2011; Washino et al., 2009). These inconsistencies among human studies stress the need for additional research to assess the potential impact of exposures to PFAS, especially in children, a vulnerable segment of the population.

Dietary intake, indoor air and house dust, drinking water, and use of products containing PFAS are potential sources of exposure to these compounds (ATSDR, 2015; DeWitt, 2015). Of late, PFAS have been detected increasingly in drinking water supplies around the world including the United States (Boiteux et al., 2012; Ericson et al., 2009; Filipovic et al., 2015; Hoffman et al., 2011; Hu et al., 2016; Post et al., 2012, 2013; Sun et al., 2016; Thompson et al., 2011; Weiss et al., 2012; Wilhelm et al., 2010), and in 2016, the U.S. Environmental Protection Agency (EPA) established a 70 parts per trillion drinking water health advisory level of PFOS and PFOA (U.S.EPA, 2016). Health advisories, which are non-enforceable and non-regulatory, provide technical guidance to state, local and tribal governments and drinking water system operators so that they can determine if concentrations of chemicals in tap water from public utilities are safe for drinking and other use. Under the U.S. EPA

Unmonitored Contaminant Monitoring Rule, from 2013 to 2016 all U.S. public water systems (PWS) serving 10,000 or more customers (and a representative sample of those serving 10,000 people) tested their supplies for six PFAS including PFOA, and PFOS. As of January 2017, of 4920 PWS with results for PFOS and PFOA, 46 (for PFOS) and 13 (for PFOA) serving millions of Americans had detections at or above the EPA's health advisory level (U.S.EPA, 2016). These findings have contributed, at least in part, to increased interest in PFAS-related research in recent years.

Assessing human exposure to PFASs can provide information useful for understanding their potential adverse health effects. Yet, PFAS data among young children (Gump et al., 2011; Harris et al., 2017; Kim et al., 2014; Pinney et al., 2014; Schecter et al., 2012; Stein and Savitz, 2011; Toms et al., 2009; Wu et al., 2015; Zhang et al., 2010), albeit important because of children's potential vulnerability to environmental insults, are not as common as data in adults. Until now, information on the extent of PFAS exposure among children in the United States was limited to a convenience group of 200 Texas children (0 to < 13 years of age) sampled in 2009 (Schecter et al., 2012), and children who participated in epidemiological studies conducted to evaluate the potential health impacts of exposure to environmental contaminants, including PFAS (Gump et al., 2011; Harris et al., 2017; Pinney et al., 2014; Stein and Savitz, 2011; Wu et al., 2015).

PFAS have been measured in the U.S. National Health and Nutrition Examination Survey (NHANES) for participants 12 years of age and older since 1999–2000 (CDC, 2017). However, because the volume of serum collected from preadolescents is limited, NHANES PFAS exposure data among persons younger than 12 years are limited to one report of concentrations using pooled sera collected in NHANES 2001–2002 from children 3–11 years old (Kato et al., 2009). Having nationally-representative exposure information among young children is of public health interest in view of the recent detection of some PFAS in drinking water systems (Hu et al., 2016), and in residents, including children, of affected communities throughout the United States (Hoffman et al., 2011; Landsteiner et al., 2014; New Hampshire Department of Environmental Services, 2017; Vermont Department of Health, 2017). Therefore, we quantified PFAS in NHANES 2013–2014 children sera, and report here the first nationally representative data on the serum concentrations of 14 PFAS in the U.S. general population 3–11 years of age, stratified by age group, sex, and race/ethnicity.

2. Materials and methods

2.1. Survey design

NHANES, conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC), is an ongoing survey designed to measure the health and nutritional status of the civilian noninstitutionalized U.S. population (CDC, 2014). The survey includes household interviews, standardized physical examinations, and collection of medical histories and biologic specimens, some of which are used to assess exposure to environmental chemicals (CDC, 2014). The NCHS Research Ethics Review Board reviewed and approved the NHANES study protocol. Parents or guardians provided written consent for all participants < 18 years of age (CDC, 2014).

For this study, we quantified 14 PFAS in serum, originally collected for the measurement of cotinine, from a random one-third subsample of 639 NHANES 2013–2014 participants 3–11 years of age. Because the subsample was random, the representative design of the survey was maintained. The sera had been shipped on dry ice to CDC's National Center for Environmental Health where it was stored at or below -20°C until analysis.

2.2. Laboratory method

We used a modification of a published on-line solid-phase extraction coupled to high-performance liquid chromatography–isotope dilution–tandem mass spectrometry (on-line SPE-HPLC–MS/MS) approach (CDC, 2016) to quantify the following 14 PFAS: perfluorooctane sulfonamide (FOSA, PFOSA), 2-(*N*-methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA, Me-PFOSA-AcOH), 2-(*N*-ethyl-perfluorooctane sulfonamido) acetic acid (EtFOSAA, Et-PFOSA-AcOH), perfluorobutane sulfonic acid (PFBS), perfluorohexane sulfonic acid (PFHxS), per-fluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluorododecanoic acid (PFDoDA), linear PFOA (n-PFOA), sum of branched isomers of PFOA (Sb-PFOA), linear PFOS (n-PFOS), and sum of perfluoromethylheptane sulfonate isomers (Sm-PFOS). Briefly, after dilution with formic acid and addition of stable isotope internal standards, one aliquot of 50 μL of serum was injected into a commercial online SPE Symbiosis system (Spark Holland, Plainsboro, NJ) for the preconcentration of the analytes on a HySphere C8-SE (7 μm) cartridge (i-Chrome solutions, Plainsboro, NJ). The analytes were then backeluted onto a pair of Chromolith[®] HighResolution RP-18e columns (4.6 \times 100 mm, Merck KGaA, Germany) for HPLC separation, and detected by negative-ion TurboIonSpray-MS/MS on an ABSciex 5500 or ABSciex 6500 Q trap mass spectrometer (Applied Biosystems, Foster City, CA). The limits of detection (LODs) were 0.1 ng/mL for all analytes. The method accuracy, calculated from the recovery at three spiking levels, ranged from 90% to 113%. We prepared low-concentration and high-concentration quality control materials (QCL and QCH, respectively) after spiking pools of commercial calf serum, and analyzed these QCs with standards, reagent and serum blanks, and NHANES samples. The precision of the measurements, expressed as the relative standard deviation of inter- and intra-day measurements of those QCs in a period of approximately 6 months, varied from 7.4% to 15.8% (QCL) and 6.3% to 11.9% (QCH), depending on the analytes. Adequate performance and accuracy of the method have been further confirmed by successful ongoing participation in two international interlaboratory comparison programs, namely the German External Quality Assessment Scheme (G-EQUAS) for PFOS and PFOA in serum, organized and managed by the Institute and Outpatient clinic for Occupational, Social and Environmental Medicine of the University of Erlangen-Nuremberg in Germany (since 2006), and the Arctic Monitoring and Assessment Program (AMAP) Ring Test, conducted by the Institut National de Santé Publique du Québec in Canada, for several PFAS, including PFHxS, PFOS, PFOA, and PFNA, in serum (since 2010). Details of the analytical method and quality assurance/QC procedures used are available on the NHANES website (CDC, 2016).

2.3. Statistical analysis

We used SAS (version 9.3; SAS Institute Inc., Cary, NC) and SUDAAN (version 11; Research Triangle Institute, Research Triangle Park, NC). SUDAAN incorporates sample weights and design variables to account for the complex design of NHANES. As recommended by NCHS, we used the subsample population WTSS2YR weights to produce estimates that are representative of the U.S. population. We used sampling weights and variance estimation (Taylor Series Linearization Method) appropriate for the complex survey design; estimates of the proportion of detectable results were also weighted. We defined two major racial/ethnic groups based on self-reported data: Hispanic (includes Mexican American and Other Hispanic) and non-Hispanic (includes non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and other race, including multiracial). We categorized age in two groups: 3–5 and 6–11 years. Participants-reported annual household income, available in \$5000 increments, ranged from < \$5000 to > \$75,000; to obtain comparable number of participants by income group, we categorized income as < \$45,000 and > \$45,000. We calculated body mass index (BMI) in Kg/m^2 using participants' weight and height, and calculated BMI percentiles for age and sex using CDC reference data (CDC, 2002). We classified BMI weight status category as underweight (< 5%), normal weight (5–< 85%), overweight (85–< 95%), or obese (≥ 95%) (CDC, 2015), and used two BMI groups to obtain comparable number of participants: underweight/ normal weight (<85%) and overweight/obese (≥ 85%). Statistical significance was set at $p < 0.05$. For PFAS concentrations below the LOD, as recommended for the analysis of NHANES data, we used a value equal to the LOD divided by the square root of 2 (Hornung and Reed, 1990). We also summed the concentrations of branched and linear isomers of PFOA and PFOS to obtain the “total” concentrations: $\Sigma\text{PFOS} = \text{Sm-PFOS} + \text{n-PFOS}$, $\Sigma\text{PFOA} = \text{Sb-PFOA} + \text{n-PFOA}$ (CDC, 2017). We replaced any isomer concentration < LOD with the imputed value before estimating the sum.

We calculated geometric means (GM) for ΣPFOS , ΣPFOA and only for analytes detected in 60% of the samples (CDC, 2017), and select percentiles, and 95% confidence intervals (CI) for ΣPFOS , ΣPFOA , and the other 14 PFAS for the total number of participants and by sex, race/ ethnicity, and age groups described above. We also calculated the correlations among the PFAS \log_{10} concentrations for analytes with detection frequencies above 60%.

We conducted weighted univariate analyses (one way ANOVA) and multivariable linear regression using the log transformed concentrations of ΣPFOS , ΣPFOA , and five other PFAS detectable in at least 60% of participants by age group, sex, race/ethnicity category, BMI, and household income. We included age group, sex, race/ethnicity category, and, because of the small degrees of freedom, either BMI or household income in the multivariable linear regression. To reach the final multivariable regression models, we used backward elimination including all the two-way interaction terms, with a threshold of $p < 0.05$ for retaining the variable in a model, using Satterwaite-adjusted F statistics. We evaluated potential effect modifiers by adding one by one each of the excluded variables into the model and examining changes in the β coefficients of the statistically significant main effects. If addition of one of these excluded variables caused a change in a β coefficient by 10%, the variable was re-added to the model.

3. Results and discussion

We quantified 14 PFAS in 639 sera collected from a nationally-representative random one-third subsample of participants 3–11 years of age from NHANES 2013–2014. Among the samples analyzed, 181 (weighted 32.67%) were from children 3–5 years old, 343 (weighted 51.32%) were from boys, 220 (weighted 24.78%) were from Hispanics, 374 (weighted 48.38%) were from children whose family reported a household income below \$45,000, and 409 (weighted 68%) were from children underweight or with a normal BMI. The GM and select percentiles of serum concentrations, sample size, and weighted detection frequency by demographic characteristics for Σ PFOS, Σ PFOA, and the 14 quantified PFAS are in Tables 1–4 and S1–S12.

We detected n-PFOA, n-PFOS, Sm-PFOS, PFHxS, and PFNA in all children (Tables 3–4, Tables S1–S3). By contrast, we detected other PFAS not as frequently (Tables S4–S12): MeFOSAA (53%), PFDA (47%), Sb-PFOA and PFUnDA (28%), PFHpA (19%), PFBS (5%), FOSA and EtFOSAA (3%), and PFDoDA (0%). The PFAS concentrations among these young children agreed relatively well with those reported among the U.S. general population of adolescents and adults during the same time period (CDC, 2017).

The GM (95% CI) concentrations (in ng/mL) of Σ PFOS and Σ PFOA were 3.88 (3.53–4.27), and 1.92 (1.75–2.12), respectively (Tables 1–2), and of the most frequently detected PFAS were: 2.51 (2.30–2.74) for n-PFOS, 1.81 (1.64–2.01) for n-PFOA, 1.23 (1.09–1.40) for Sm-PFOS, 0.843 (0.756–0.939) for PFHxS, and 0.794 (0.681–0.926) for PFNA (Tables 3–4 and S1–S4). Electrochemical fluorination (ECF) used in the United States from the 1950s until the early 2000s to manufacture PFAS, including PFOA and PFOS, yielded branched and linear isomers. After 3 M, the largest PFOS manufacturer worldwide, voluntarily stopped production of PFOS, PFOS precursors, and related compounds (including PFHxS and PFOA) in 2002, telomerization which produces almost exclusively linear compounds, replaced ECF (ATSDR, 2015; DeWitt, 2015). The detection of Sm-PFOS in all children and of Sb-PFOA in approximately a quarter of them suggests exposure to PFAS produced by ECF, even among children born approximately a decade after discontinued ECF production in the United States. In these NHANES 2013–2014 children, Sm-PFOS was approximately 1/3 of Σ PFOS, a proportion similar to that among adolescent (12–19 years of age) and adult (>20 years of age) NHANES 2013–2014 participants (CDC, 2017). Children's exposure to branched PFOS/PFOA isomers may have occurred early in life during gestation because PFAS can cross the placenta (Apelberg et al., 2007; ATSDR, 2015; Cariou et al., 2015; Chen et al., 2017; DeWitt, 2015; Kato et al., 2014; Lee et al., 2013; Porpora et al., 2013; Yang et al., 2016) or during infancy through breastfeeding, a known PFAS exposure pathway (Antignac et al., 2013; ATSDR, 2015; Cariou et al., 2015; DeWitt, 2015; Forns et al., 2015; Kang et al., 2016; Mondal et al., 2014). However, with the available information, we cannot rule out postnatal exposure to branched isomers through use of consumer products manufactured before the changes in PFAS production in the United States or that are still manufactured elsewhere by the ECF process (Xie et al., 2013).

These NHANES data confirm previous reports of exposure to several PFAS in U.S. children (Harris et al., 2017; Pinney et al., 2014; Schecter et al., 2012; Wu et al., 2015), including

children exposed to PFAS from consumption of drinking water accidentally contaminated with PFAS (Mondal et al., 2012; New Hampshire Department of Environmental Services, 2017; Stein and Savitz, 2011). Compared with these other studies in most of which serum or plasma samples were collected years ago, the GM concentrations of Σ PFOS, Σ PFOA, PFHxS and PFNA in NHANES 2013–2014 participants 3–11 years of age were among the lowest (Fig. 1). As expected, concentrations of PFOS, PFOA, and PFHxS were generally higher in children whose samples were collected in the mid- to late-2000s, after production and/or emissions of PFOS, PFOA, and related chemistries were expected to decline in the United States (ATSDR, 2015; Wang et al., 2017). Of interest, concentrations (GM or median) of PFOA were highest among children who participated in the C8 study, a project involving residents in Mid-Ohio Valley communities who consumed drinking water contaminated with PFOA from factory emissions of a nearby manufacturing plant (Frisbee et al., 2009; Mondal et al., 2012). Similarly, although samples were collected in 2015, children < 12 years of age who consumed PFAS-contaminated drinking water at the Pease International Tradeport in New Hampshire had GM concentrations of PFOS, PFOA, and PFHxS considerably higher than those from NHANES 2013–2014 children and similar to those reported for other populations of U.S. children known to have been exposed to PFAS through consumption of contaminated drinking water (Mondal et al., 2012; New Hampshire Department of Environmental Services, 2017; Pinney et al., 2014).

Among NHANES 2013–2014 children, we observed statistically significant (all $p < 0.01$) correlations between the log-transformed concentrations of Sm-PFOS and n-PFOS (Pearson correlation coefficient (r) = 0.60), n-PFOA (r = 0.46), and PFHxS (r = 0.52); between n-PFOA and n-PFOS (r = 0.50), and PFHxS (r = 0.45); and between n-PFOS and PFHxS (r = 0.58) (Table S13). Correlations of PFNA with the other four PFAS were also statistically significant (all $p < 0.01$) but not as strong (Table S13): Sm-PFOS (r = 0.27); n-PFOA (r = 0.39); n-PFOS (r = 0.35); PFHxS (r = 0.24). The relatively strong correlations between Sm-PFOS, n-PFOS, n-PFOA, and PFHxS, and to a lesser extent, PFNA, suggest similar or common background source(s) or pathway(s) of exposure among the general population for these PFAS, as also suggested from previous NHANES results (Calafat et al., 2007a).

The GM concentrations from the weighted univariate regression analyses of Σ PFOS, Σ PFOA, and the five PFAS (n-PFOA, n-PFOS, Sm-PFOS, PFHxS, and PFNA) detected in at least 60% of participants are shown in Table 5. For Σ PFOS and Sm-PFOS, non-Hispanics had significantly higher (p = 0.0324 and 0.0483, respectively) GMs than Hispanics, and children 6–11 years old had higher GMs than the 3–5 year olds (p = 0.0004 and 0.0005, respectively); GMs by sex, BMI, or household income did not differ significantly (Table S14). GM concentrations of n-PFOS were significantly higher among the 6–11 year olds compared to the younger children (p = 0.0016); differences by race/ethnicity, sex, BMI, or household income did not reach statistical significance (Table S14). Similarly, for Σ PFOA and n-PFOA, GM concentrations were higher in non-Hispanic compared to Hispanic children (p = 0.0038 and 0.0045, respectively); GMs by age group, or sex did not differ significantly, and differences by BMI or household income were of borderline significance (Table S14). For PFHxS, 6–11 year olds had higher GM concentrations than the 3–5 year olds (p = 0.0119), and boys had higher GM concentrations than girls (p = 0.0035); we observed no significant differences by race/ethnicity, BMI or household income (Table S14).

We did not observe significant differences in PFNA GMs by age, sex, race/ethnicity, BMI, or income (Table S14).

The final multivariate regression models did not retain BMI or household income for any of the biomarkers examined (Table 6). Instead, the final models included race/ethnicity, age, sex, age \times race/ethnicity, age \times sex for Σ PFOS; age, sex, age \times sex for n-PFOS; race/ethnicity, age, and age \times race/ethnicity for Sm-PFOS; race for Σ PFOA and n-PFOA; and age and sex for PFHxS; we found no association between the demographic variables evaluated and PFNA (Tables 6 and S14). For Σ PFOS and n-PFOS, 6–11 year olds had significantly higher adjusted GM concentration than 3–5 year olds, but only among boys ($p = 0.0003$ and 0.0017 , respectively), and 6–11 year old boys had significantly higher adjusted GM concentrations than girls 6–11 years of age ($p = 0.0048$ and 0.0016 , respectively). Similarly, for Sm-PFOS, 6–11 year olds had significantly higher adjusted GM than 3–5 year olds, but only among non-Hispanic children ($p = 0.0005$), and Hispanic 6–11 year old children had significantly lower concentrations than non-Hispanics ($p = 0.0006$). Regardless of age, Hispanic children had significantly lower Σ PFOA ($p = 0.0038$) and n-PFOA ($p = 0.0045$) than non-Hispanics. Children 6–11 years of age had higher adjusted GM concentrations of PFHxS than younger children ($p = 0.0123$), and boys had higher concentrations than girls (0.0047).

The multivariate regression analyses suggested higher concentrations of PFOS (Σ PFOS, n-PFOS, Sm-PFOS) and PFHxS in older compared to younger children (Tables 6 and S14); these associations were modified by sex and/or race/ethnicity. Concentrations of some PFAS were previously reported to increase with age (Haug et al., 2009; Karrman et al., 2006; Kim et al., 2014; Schecter et al., 2012), partially due to the persistence of these chemicals in the environment and in humans. It is also possible that younger persons were exposed to lower levels of PFOS and PFHxS than older people because of changes in PFAS manufacturing practices since the early 2000s (ATSDR, 2015; DeWitt, 2015). However, the positive association between age and PFAS in people was not always evident (Calafat et al., 2007a; Kannan et al., 2004; Kato et al., 2009; Zhang et al., 2010), as our study also suggested that age was only positively associated with Σ PFOS and n-PFOS in boys, but not in girls; and in non-Hispanics, but not in Hispanics for Sm-PFOS. Age was not even associated with Σ PFOA and n-PFOA concentrations.

The multivariate regression analyses suggesting associations with race/ethnicity for PFOA and PFOS (Tables 6 and S14), agree with previous nationally-representative NHANES data (Calafat et al., 2007a) which showed that Mexican Americans had lower concentrations of PFOA and PFOS than persons of non-Hispanic race. Racial differences in PFAS concentrations may relate to lifestyle, diet, and use of PFAS-containing products. Furthermore, the multivariate regression analyses suggested associations with sex for PFHxS, and with sex and age or race/ethnicity for PFOS. Concentrations of some PFAS in adults have been reported to differ with sex, with adult males having higher concentrations than adult females (Calafat et al., 2007a,b; Fromme et al., 2007; Holzer et al., 2008; Yeung et al., 2006) because women may decrease their PFAS body burden through gestation, breastfeeding, or menstruation (ATSDR, 2015; DeWitt, 2015). However, an association by sex was not observed before in children, including studies using data from pooled sera

collected from NHANES 2001–2002 children (Kato et al., 2009) or from infants and children in Queensland, Australia (Toms et al., 2009), and from individual sera collected from a convenience group of Texas infants and children between 0 and 12 years of age (Schechter et al., 2012), and from South Korea children 5–13 years of age (Kim et al., 2014). The sex-related associations for PFOS and PFHxS concentrations among NHANES 2013–2014 children are difficult to explain because factors that support lower PFAS concentrations in women compared to men (i.e., gestation, breastfeeding, menstruation) are not expected to apply to young age children.

The GM concentrations of Σ PFOS and Σ PFOA in these 3–11 year olds from NHANES 2013–2014 (Tables 1–2) were comparable to the GM concentrations among NHANES 2013–2014 adolescent and adult participants (CDC, 2017). The GM concentration (95% CI) of Σ PFOS was significantly higher in NHANES 2013–2014 participants 12 years and older [4.99 (4.50–5.52) ng/mL] than in children 3–11 years of age [3.88 (3.53–4.27) ng/mL]. However, for Σ PFOA GMs (95% CI) were similar [1.94 (1.76–2.14) ng/mL for persons 12 years and older, and 1.92 (1.75–2.12) ng/mL for 3–11 years old]. The Σ PFOS upward trend with age may relate to the fact that older persons would have experienced past higher exposures to PFOS than these young children because the largest PFOS manufacturer stopped production of PFOS in 2002 (ATSDR, 2015; DeWitt, 2015). By contrast, the lack of an age trend for Σ PFOA may be explained by the ongoing production of PFOA, PFOA precursors (e.g., fluorotelomer-based compounds (Butt et al., 2014)), and related homolog chemicals at the time of NHANES 2013–2014—even though environmental emissions and product content levels of these chemicals were substantially reduced since 2006 thanks in part to the 2010/2015 PFOA Stewardship Program, a partnership between the U.S. EPA and eight major companies in the PFAS industry (ATSDR, 2015; DeWitt, 2015; US EPA, 2006).

In summary, we present the first nationally representative data on the serum concentrations of 14 PFAS in the U.S. general population 3–11 years of age, stratified by age group, sex, and race/ethnicity. The detection of five PFAS (n-PFOS, Sm-PFOS, n-PFOA, PFHxS, PFNA) in all samples analyzed and the similar GM concentrations of these PFAS in 3–11 year old children as in adolescents and adults participating in NHANES 2013–2014 confirm widespread exposure to these PFAS even among young Americans. Even children born after the major U.S. manufacturer voluntarily discontinued ECF production in 2002 of PFOS precursors and related compounds in the United States were exposed to PFAS manufactured by ECF. The reported PFAS concentration differences by sex, race/ethnicity, and age highlight the need for additional research to identify sources of human exposure to PFAS and to study the environmental fate and transport of these chemicals. Last, these NHANES data can be used to establish a nationally representative baseline of exposures to PFAS among pre-school and elementary-school aged children that can be used to identify higher-than background exposures among children throughout the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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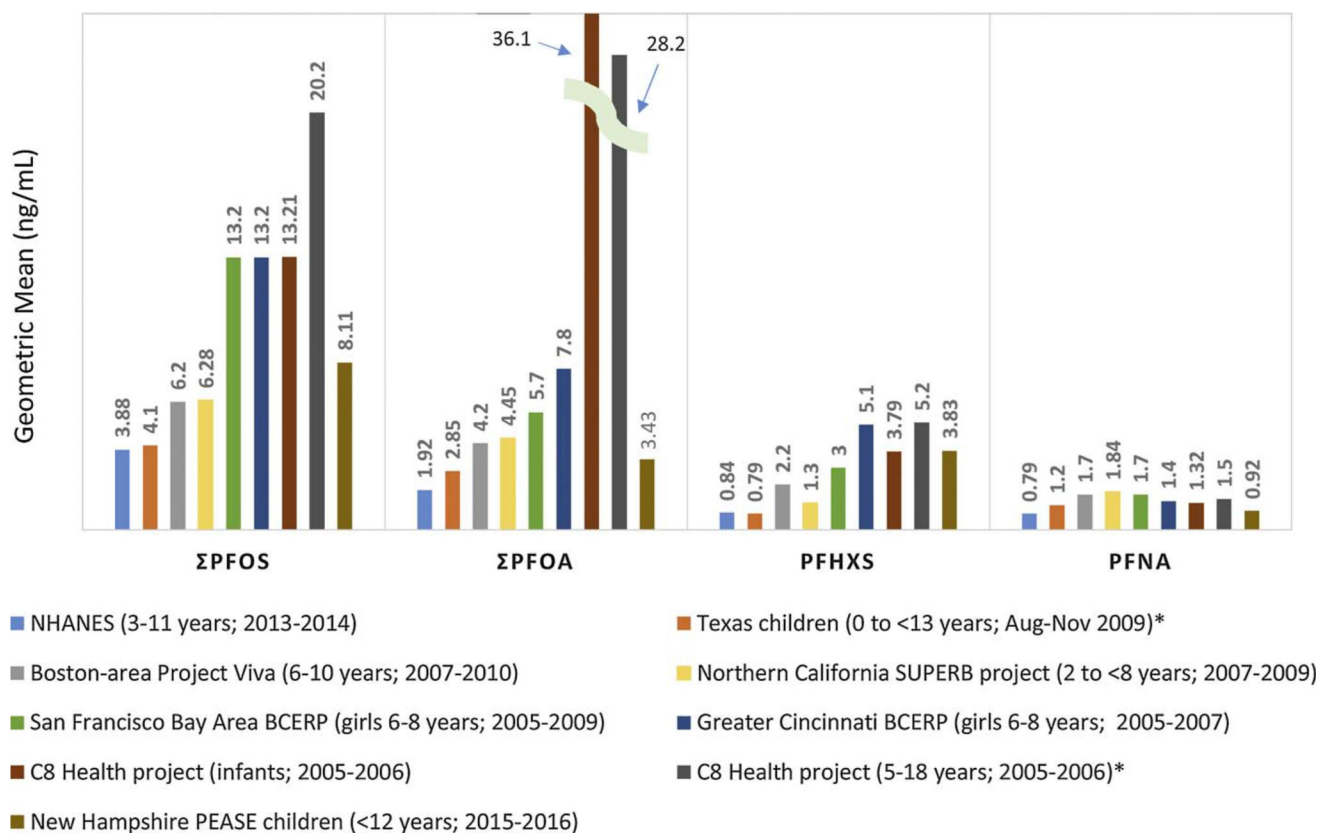


Fig. 1.

Comparison of geometric mean concentrations of ΣPFOS, ΣPFOA, PFHxS, and PFNA in several groups of U.S. children: U.S. general population of 3–11 years (this work), Texas children (N = 200) 0 to < 13 years* (Schechter et al., 2012), Boston-area Project Viva children (N = 653) 6–10 years (Harris et al., 2017), Northern California SUPERB study children (N = 68) 2 to < 8 years (Wu et al., 2015), Greater Cincinnati BCERP girls (N = 353) 6–8 years (Pinney et al., 2014), San Francisco Bay Area BCERP girls (N = 351) 6–8 years (Pinney et al., 2014), New Hampshire PEASE children (N = 366) <12 years (New Hampshire Department of Environmental Services, 2017), C8 Health Project infants (N = 49) (Mondal et al., 2014), and C8 Health Project children (N = 10,546) 5–18 years* (Stein and Savitz, 2011).

*Denotes that concentrations are medians.

Table 1

Geometric mean, select percentiles of total serum concentrations of PFOS isomers (Σ PFOS) [ng/mL (95% CI)], and sample size by demographic characteristics in the U.S. population 3–11 years of age from NHANES 2013–2014.

	Survey years	Geometric mean		Selected percentile (95% confidence interval)			Sample size
		(95% confidence interval)		50th	75th	90th	
Total	13–14	3.88 (3.53–4.27)	3.75 (3.44–4.17)	5.56 (4.83–6.33)	7.99 (7.03–9.53)	11.0 (9.03–12.4)	639
Age group							
3–5 years	13–14	3.38 (3.04–3.77)	3.41 (2.84–3.78)	4.78 (3.98–6.32)	7.18 (5.50–8.71)	8.82 (7.18–11.0)	181
6–11 years	13–14	4.15 (3.76–4.58)	4.02 (3.54–4.45)	5.77 (5.10–6.43)	8.78 (6.75–11.8)	12.4 (9.32–14.1)	458
Gender							
Males	13–14	4.07 (3.56–4.65)	4.13 (3.44–4.76)	6.19 (5.29–7.18)	8.78 (7.18–11.8)	11.8 (8.01–15.4)	343
Females	13–14	3.70 (3.38–4.06)	3.54 (3.24–3.96)	4.88 (4.45–5.70)	7.02 (6.33–8.71)	9.44 (7.17–12.0)	296
Race/ethnicity							
Hispanic	13–14	3.53 (3.13–3.99)	3.41 (2.95–3.84)	4.71 (4.13–5.65)	7.60 (5.43–9.44)	9.32 (6.50–11.0)	220
Non-Hispanic	13–14	4.01 (3.62–4.44)	3.96 (3.44–4.48)	5.97 (5.02–6.49)	8.06 (6.98–11.3)	12.0 (9.10–13.6)	419

Geometric mean, select percentiles of total serum concentrations of PFOA isomers (Σ PFOA) [ng/mL (95% CI)], and sample size by demographic characteristics in the U.S. population 3–11 years of age from NHANES 2013–2014.

Table 2

	Survey years	Geometric Mean		Selected percentile (95% confidence interval)					Sample size			
		(95% confidence interval)		50th	75th	90th	95th					
Total	13–14	1.92	(1.75–2.12)	1.94	(1.66–2.15)	2.67	(2.42–2.88)	3.53	(3.13–4.09)	4.19	(3.62–5.47)	639
Age group												
3–5 years	13–14	2.00	(1.75–2.29)	1.80	(1.62–2.40)	2.94	(2.66–3.28)	4.14	(2.88–5.86)	5.58	(3.28–7.02)	181
6–11 years	13–14	1.89	(1.72–2.07)	1.94	(1.68–2.14)	2.53	(2.25–2.84)	3.26	(2.97–3.68)	3.84	(3.40–4.09)	458
Gender												
Males	13–14	1.95	(1.76–2.15)	1.90	(1.64–2.19)	2.71	(2.39–3.26)	3.62	(3.23–4.00)	4.14	(3.41–5.86)	343
Females	13–14	1.90	(1.68–2.14)	1.94	(1.63–2.18)	2.55	(2.30–2.80)	3.30	(2.88–4.01)	4.22	(3.07–5.47)	296
Race/ethnicity												
Hispanic	13–14	1.71	(1.56–1.88)	1.68	(1.55–1.93)	2.31	(2.05–2.60)	2.91	(2.48–3.30)	3.29	(2.86–4.00)	220
Non-Hispanic	13–14	2.00	(1.79–2.23)	1.99	(1.71–2.34)	2.75	(2.50–3.16)	3.72	(3.20–4.22)	4.28	(3.79–5.86)	419

Geometric mean, selected percentiles of serum concentrations of PFHxS [ng/mL (95% CI)], sample size, and weighted percent detection frequency by demographic characteristics in the U.S. population 3–11 years of age from NHANES 2013–2014.

Table 3

	Survey years	Geometric Mean		Selected percentile (95% confidence interval)			Sample size	Weighted Detection Percent
		(95% confidence interval)		50th	75th	90th		
Total	13–14	0.843 (0.756–0.939)	0.810 (0.710–0.900)	1.24 (1.08–1.47)	2.14 (1.62–2.81)	3.12 (2.29–4.59)	639	100
Age group								
3–5 years	13–14	0.715 (0.617–0.828)	0.740 (0.580–0.830)	1.04 (0.920–1.24)	1.55 (1.07–2.41)	1.62 (1.31–3.66)	181	100
6–11 years	13–14	0.913 (0.803–1.04)	0.850 (0.730–0.960)	1.41 (1.13–1.65)	2.33 (1.84–3.20)	4.14 (2.33–6.42)	458	100
Gender								
Males	13–14	0.933 (0.813–1.07)	0.930 (0.770–1.02)	1.54 (1.24–1.59)	2.32 (1.64–3.70)	3.73 (2.32–5.97)	343	100
Females	13–14	0.757 (0.672–0.853)	0.740 (0.620–0.830)	1.03 (0.930–1.19)	1.65 (1.41–2.26)	2.94 (1.75–3.74)	296	100
Race/ethnicity								
Hispanic	13–14	0.787 (0.697–0.890)	0.740 (0.640–0.810)	1.13 (1.01–1.39)	2.20 (1.31–3.20)	2.81 (1.88–5.89)	220	100
Non-Hispanic	13–14	0.862 (0.761–0.977)	0.840 (0.710–0.940)	1.29 (1.08–1.55)	2.14 (1.62–3.02)	3.56 (2.32–4.74)	419	100

Geometric mean, select percentiles of serum concentrations of PFNA [ng/mL (95% CI)], sample size, and weighted percent detection frequency by demographic characteristics in the U.S. population 3–11 years of age from NHANES 2013–2014.

Table 4

	Survey years	Geometric Mean		Selected percentile (95% confidence interval)			Sample size	Weighted Detection Percent
		(95% confidence interval)		50th	75th	90th		
Total	13–14	0.794 (0.681–0.926)	0.700 (0.610–0.820)	1.08 (0.920–1.35)	2.03 (1.29–3.42)	3.26 (1.94–5.35)	639	100
Age group								
3–5 years	13–14	0.764 (0.630–0.928)	0.620 (0.540–0.760)	1.11 (0.840–1.53)	2.03 (1.21–5.03)	3.49 (1.41–7.95)	181	100
6–11 years	13–14	0.809 (0.682–0.960)	0.750 (0.630–0.860)	1.07 (0.920–1.38)	1.98 (1.16–3.56)	3.19 (1.55–4.88)	458	100
Gender								
Males	13–14	0.829 (0.686–1.00)	0.720 (0.610–0.850)	1.10 (0.890–1.59)	2.34 (1.17–5.35)	3.85 (1.72–6.93)	343	100
Females	13–14	0.759 (0.638–0.902)	0.680 (0.570–0.870)	1.07 (0.890–1.35)	1.88 (1.21–2.84)	2.58 (1.42–4.06)	296	100
Race/ethnicity								
Hispanic	13–14	0.753 (0.622–0.912)	0.640 (0.540–0.760)	1.03 (0.790–1.53)	1.98 (1.15–3.26)	3.00 (1.59–9.32)	220	100
Non-Hispanic	13–14	0.808 (0.681–0.958)	0.720 (0.600–0.870)	1.09 (0.920–1.38)	2.08 (1.34–3.47)	3.46 (1.88–5.35)	419	100

Table 5

Geometric mean concentrations (95% CI) in ng/mL of Σ PFOS, n -PFOS, Sm-PFOS, Σ PFOA, n -PFOA, PFHxS, and PFNA by race/ethnicity, age group, sex, BMI, and household income from weighted univariate analyses.

Variable	Σ PFOS	n -PFOS	Sm-PFOS	Σ PFOA	n -PFOA	PFHxS	PFNA
Race/ethnicity							
Hispanic	3.53 (3.13–3.98)	2.29 (2.00–2.61)	1.13 (1.00–1.27)	1.71 (1.56–1.88)	1.61 (1.47–1.78)	0.79 (0.70–0.89)	0.75 (0.62–0.91)
Non-Hispanic	4.01 (3.62–4.44)	2.59 (2.35–2.85)	1.27 (1.10–1.46)	2.00 (1.79–2.23)	1.88 (1.68–2.11)	0.86 (0.76–0.98)	0.81 (0.68–0.96)
Age group							
3–5 years	3.38 (3.04–3.77)	2.22 (2.01–2.46)	1.03 (0.87–1.21)	2.00 (1.75–2.29)	1.87 (1.62–2.17)	0.72 (0.62–0.83)	0.76 (0.63–0.93)
6–11 years	4.15 (3.76–4.58)	2.67 (2.43–2.92)	1.35 (1.19–1.52)	1.89 (1.72–2.07)	1.78 (1.61–1.97)	0.91 (0.80–1.04)	0.81 (0.68–0.96)
Sex							
Male	4.07 (3.56–4.65)	2.67 (2.33–3.06)	1.26 (1.08–1.48)	1.95 (1.76–2.15)	1.83 (1.65–2.04)	0.93 (0.81–1.07)	0.83 (0.69–1.00)
Female	3.70 (3.37–4.05)	2.36 (2.19–2.53)	1.20 (1.04–1.39)	1.90 (1.68–2.14)	1.79 (1.57–2.03)	0.76 (0.67–0.85)	0.76 (0.64–0.90)
BMI							
Underweight/normal	3.99 (3.57–4.46)	2.58 (2.34–2.83)	1.26 (1.07–1.48)	2.01 (1.80–2.25)	1.89 (1.68–2.14)	0.87 (0.78–0.98)	0.78 (0.68–0.89)
Overweight/obese	3.69 (3.25–4.18)	2.39 (2.09–2.74)	1.18 (1.03–1.34)	1.75 (1.54–1.99)	1.65 (1.45–1.89)	0.79 (0.68–0.90)	0.83 (0.64–1.08)
Household income							
< \$45,000	3.78 (3.41–4.20)	2.49 (2.24–2.77)	1.16 (1.02–1.32)	1.78 (1.57–2.02)	1.67 (1.46–1.92)	0.86 (0.76–0.97)	0.78 (0.69–0.88)
> \$45,000	4.01 (3.57–4.51)	2.54 (2.29–2.83)	1.33 (1.12–1.57)	2.06 (1.85–2.30)	1.96 (1.75–2.19)	0.85 (0.74–0.97)	0.81 (0.67–0.99)

Table 6

Least square geometric mean concentrations (95% CI) in ng/mL of Σ PFOS, Sm-PFOS, n-PFOS, Σ PFOA, n-PFOA, and PFHxS for the significant variables from the multiple regression models^a.

	Σ PFOS	nPFOS	Sm-PFOS	Σ PFOA	n-PFOA	PFHxS
3–5 years						0.71 (0.62–0.83)
6–11 years						0.91 (0.80–1.04)
Male						0.93 (0.82–1.07)
Female						0.76 (0.67–0.85)
Hispanic				1.71 (1.56–1.88)	1.61 (1.47–1.78)	
Non-Hispanic				2.00 (1.79–2.23)	1.88 (1.68–2.11)	
3–5 years, Hispanic	3.44 (2.99–3.95)		1.11 (0.94–1.31)			
6–11 years, Hispanic	3.58 (3.15–4.07)		1.13 (1.01–1.27)			
3–5 years, non-Hispanic	3.37 (2.97–3.82)		1.00 (0.82–1.22)			
6–11 years, non-Hispanic	4.36 (3.92–4.84)		1.42 (1.25–1.61)			
Male, 3–5 years	3.28 (2.78–3.86)	2.18 (1.83–2.60)				
Female, 3–5 years	3.50 (3.09–3.96)	2.27 (2.01–2.55)				
Male, 6–11 years	4.52 (3.96–5.17)	2.95 (2.57–3.40)				
Female, 6–11 years	3.79 (3.45–4.17)	2.40 (2.22–2.59)				

^aThe final multivariate regression models included: race/ethnicity, age, sex, age \times race/ethnicity, age \times sex (Σ PFOS); age, sex, age \times sex (n-PFOS); race/ethnicity, age, and age \times race/ethnicity (Sm-PFOS); race (Σ PFOA and n-PFOA); and age and sex (PFHxS). We found no association between the demographic variables evaluated and PFNA.